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NEWS 4	Aug 08	PHARMAMarketLetter(PHARMAML) - new on STN
NEWS 5	Aug 19	Aquatic Toxicity Information Retrieval (AQUIRE) now available on STN
NEWS 6	Aug 26	Sequence searching in REGISTRY enhanced
NEWS 7	Sep 03	JAPIO has been reloaded and enhanced
NEWS 8	Sep 16	Experimental properties added to the REGISTRY file
NEWS 9	Sep 16	CA Section Thesaurus available in CAPLUS and CA
NEWS 10	Oct 01	CASREACT Enriched with Reactions from 1907 to 1985
NEWS 11	Oct 24	BEILSTEIN adds new search fields
NEWS 12	Oct 24	Nutraceuticals International (NUTRACEUT) now available on STN
NEWS 13	Nov 18	DKILIT has been renamed APOLLIT
NEWS 14	Nov 25	More calculated properties added to REGISTRY
NEWS 15	Dec 04	CSA files on STN
NEWS 16	Dec 17	PCTFULL now covers WP/PCT Applications from 1978 to date
NEWS 17	Dec 17	TOXCENTER enhanced with additional content
NEWS 18	Dec 17	Adis Clinical Trials Insight now available on STN
NEWS 19	Jan 29	Simultaneous left and right truncation added to COMPENDEX, ENERGY, INSPEC
NEWS 20	Feb 13	CANCERLIT is no longer being updated
NEWS 21	Feb 24	METADEX enhancements
NEWS 22	Feb 24	PCTGEN now available on STN
NEWS 23	Feb 24	TEMA now available on STN
NEWS 24	Feb 26	NTIS now allows simultaneous left and right truncation
NEWS 25	Feb 26	PCTFULL now contains images
NEWS 26	Mar 04	SDI PACKAGE for monthly delivery of multifile SDI results
NEWS 27	Mar 20	EVENTLINE will be removed from STN
NEWS 28	Mar 24	PATDPAFULL now available on STN
NEWS 29	Mar 24	Additional information for trade-named substances without structures available in REGISTRY
NEWS 30	Apr 11	Display formats in DGENE enhanced
NEWS 31	Apr 14	MEDLINE Reload
NEWS 32	Apr 17	Polymer searching in REGISTRY enhanced
NEWS 33	Jun 13	Indexing from 1947 to 1956 added to records in CA/CAPLUS
NEWS 34	Apr 21	New current-awareness alert (SDI) frequency in WPIDS/WPINDEX/WPIX
NEWS 35	Apr 28	RDISCLOSURE now available on STN
NEWS 36	May 05	Pharmacokinetic information and systematic chemical names added to PHAR
NEWS 37	May 15	MEDLINE file segment of TOXCENTER reloaded
NEWS 38	May 15	Supporter information for ENCOMPPAT and ENCOMPLIT updated
NEWS 39	May 16	CHEMREACT will be removed from STN
NEWS 40	May 19	Simultaneous left and right truncation added to WSCA
NEWS 41	May 19	RAPRA enhanced with new search field, simultaneous left and

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                    right truncation
 NEWS 42   Jun 06  Simultaneous left and right truncation added to CBNB
 NEWS 43   Jun 06  PASCAL enhanced with additional data
 NEWS 44   Jun 20  2003 edition of the FSTA Thesaurus is now available
 NEWS 45   Jun 25  HSDB has been reloaded

 NEWS EXPRESS  April 4 CURRENT WINDOWS VERSION IS V6.01a, CURRENT
               MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP),
               AND CURRENT DISCOVER FILE IS DATED 01 APRIL 2003
 NEWS HOURS    STN Operating Hours Plus Help Desk Availability
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=> s tnfr1 or (tnf (2n) receptor (2n) 1) or (tnfr (n) 1)
L1         4881 TNFR1 OR (TNF (2N) RECEPTOR (2N) 1) OR (TNFR (N) 1)

=> s antisense or (anti (n) sense) or (complem? (2n) (oligonucl? or nucl?))
   4 FILES SEARCHED...
L2       125942 ANTISENSE OR (ANTI (N) SENSE) OR (COMPLEM? (2N) (OLIGONUCL? OR
                NUCL?))

=> s l1 and l2
L3           60 L1 AND L2

=> dup rem l3
PROCESSING COMPLETED FOR L3
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L4 25 DUP REM L3 (35 DUPLICATES REMOVED)

=> d l4 1-25 ibib abs

L4 ANSWER 1 OF 25 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 2003149666 MEDLINE
DOCUMENT NUMBER: 22552373 PubMed ID: 12517920
TITLE: Inhibition of tumor necrosis factor alpha-mediated NFkappaB activation and leukocyte adhesion, with enhanced endothelial apoptosis, by G protein-linked receptor (TP) ligands.
AUTHOR: Ashton Anthony W; Ware Gabriel M; Kaul Dhananjaya K; Ware J Anthony
CORPORATE SOURCE: Department of Medicine, Albert Einstein College of Medicine, Yeshiva University, Bronx, New York 10461, USA.
CONTRACT NUMBER: HL47032 (NHLBI)
HL51043 (NHLBI)
HL55552 (NHLBI)
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (2003 Apr 4) 278 (14) 11858-66.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200305
ENTRY DATE: Entered STN: 20030401
Last Updated on STN: 20030520
Entered Medline: 20030519

AB Tumor necrosis factor (TNF) alpha is a critical mediator of inflammation; however, TNFalpha is rarely released alone and the "cross-talk" between different classes of inflammatory mediators is largely unexplored. Thromboxane A(2) (TXA(2)) is released during I/R injury and exerts its effects via a G protein-linked receptor (TP). In this study, we found that TXA(2) mimetics stimulate leukocyte adhesion molecule (LAM) expression on endothelium via TPbeta. The potential interaction between TXA(2) and TNFalpha in altering endothelial survival and LAM expression was examined. IBOP, a TXA(2) mimetic, attenuated TNFalpha-induced LAM expression in vitro, in a concentration-dependent manner, by preventing TNFalpha-enhanced gene expression, and also reduced TNFalpha-induced leukocyte adhesion to endothelium both in vitro and in vivo. IBOP abrogated TNFalpha-induced NFkappaB activation in endothelial cells, as determined by reduced IkappaB phosphorylation and NFkappaB nuclear translocation, by inhibiting the assembly of signaling intermediates with the intracellular domain of **TNF receptors 1** and 2 in response to TNFalpha. This inhibition resulted from the Galpha(q)-mediated enhancement of STAT1 activation and was reversed by anti-STAT1 **antisense** oligonucleotides. TNFalpha-mediated **TNFR1**-FADD association and caspase 8 activation were not inhibited by IBOP co-stimulation, however, resulting in a 2.6-fold increase in endothelial cell apoptosis. By stimulating the vessel wall and inducing endothelial cell apoptosis, TXA(2), in combination with TNFalpha, may hamper the angiogenic response during inflammation or ischemia, thus reducing revascularization and tissue viability.

L4 ANSWER 2 OF 25 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 2003230898 IN-PROCESS
DOCUMENT NUMBER: 22637775 PubMed ID: 12752784
TITLE: Tumor necrosis factor receptor type-1 in sensory neurons contributes to induction of chronic enhancement of inflammatory hyperalgesia in rat.
AUTHOR: Parada Carlos A; Yeh Jenny J; Joseph Elizabeth K; Levine

Jon D
CORPORATE SOURCE: Departments of Medicine and Oral and Maxillofacial Surgery, Division of Neuroscience and Sciences Program, NIH Pain Center (UCSF), C522/Box 0440, 521 Parnassus Ave, University of California at San Francisco, San Francisco, CA 94143-0440, USA.
SOURCE: EUROPEAN JOURNAL OF NEUROSCIENCE, (2003 May) 17 (9) 1847-52.
Journal code: 8918110. ISSN: 0953-816X.
PUB. COUNTRY: France
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: IN-PROCESS; NONINDEXED; Priority Journals
ENTRY DATE: Entered STN: 20030520
Last Updated on STN: 20030520

AB Carrageenan-induced inflammatory pain lasting hours to days produces a protein kinase C epsilon (PKC varepsilon)-dependent 'primed' state lasting several weeks, during which time injection of prostaglandin E2 induces hyperalgesia which is markedly enhanced and prolonged compared to PGE2-induced hyperalgesia in normal 'unprimed' rats. In the present study, we demonstrate that while inhibition of prostaglandin synthesis and antagonism of beta2-adrenergic receptors markedly attenuated the hyperalgesia induced by carrageenan, these interventions did not affect hyperalgesic priming. Tumor necrosis factor-alpha (rat recombinant; rrTNFalpha), another mediator of carrageenan-induced inflammation, alone produced hyperalgesia and priming, which were attenuated and prevented, respectively, by intrathecal administration of **antisense** to PKC varepsilon. Inhibition of TNFalpha with thalidomide or a rat polyclonal anti-TNFalpha antibody attenuated carrageenan-induced hyperalgesia and prevented priming. Intrathecal administration of **antisense** to tumour necrosis factor receptor type-1 (**TNFR1**) reduced the level of **TNFR1** transported toward the peripheral terminals of sensory neurons, and attenuated both carrageenan- and rrTNFalpha-induced priming. Acute hyperalgesia induced by carrageenan or rrTNFalpha remained intact in animals treated with **TNFR1 antisense**. Our results demonstrate that the generation of the primed state does not require production of hyperalgesia and that TNFalpha, which is generated during acute inflammation, can act on sensory neurons to induce hyperalgesic priming by activating neuronal PKC varepsilon.

L4 ANSWER 3 OF 25 MEDLINE DUPLICATE 3
ACCESSION NUMBER: 2003230503 MEDLINE
DOCUMENT NUMBER: 22637259 PubMed ID: 12754112
TITLE: TNF-alpha induces apoptosis of parietal cells.
AUTHOR: Neu Bruno; Puschmann Andreas J; Mayerhofer Artur; Hutzler Peter; Grossmann Johannes; Lippl Florian; Schepp Wolfgang; Prinz Christian
CORPORATE SOURCE: Second Department of Medicine, Technical University of Munich, Ismaningerstr. 22, D-81675, Munich, Germany.. bruno.neu@lrz.tum.de
SOURCE: BIOCHEMICAL PHARMACOLOGY, (2003 May 15) 65 (10) 1755-60.
Journal code: 0101032. ISSN: 0006-2952.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200306
ENTRY DATE: Entered STN: 20030520
Last Updated on STN: 20030618
Entered Medline: 20030617

AB Helicobacter pylori infection can be associated with chronic gastric inflammation and hypochlorhydria with increased levels of the

proinflammatory cytokines. The current study investigated the effects of TNF-alpha on programmed death of gastric parietal cells. TNF-alpha induced apoptosis of parietal cells in isolated perfused rat stomachs at 10ng/mL. In isolated and highly enriched rat parietal cells, 10ng/mL TNF-alpha induced a 2.6-fold increase in the apoptotic rate. The 55kDa protein of **TNFR-1** but not the 75kDa of TNFR-2 was detected by Western blot analysis. TNF-alpha-induced apoptosis of isolated parietal cells was inhibited by pretreatment with different NF-kappaB-inhibitors, nitric oxide synthase inhibitors and with **antisense**-oligodeoxynucleotides against the p65 subunit of NF-kappaB. Investigation of downstream signaling pathways of apoptosis revealed that TNF-alpha induced the expression of iNOS, but failed to stimulate the activity of caspase 3. The TNF-alpha effect on gastric parietal cells may contribute to the atrophy and hypochlorhydria of the gastric mucosa observed during chronic H. pylori infection.

L4 ANSWER 4 OF 25 CA COPYRIGHT 2003 ACS
ACCESSION NUMBER: 137:57583 CA
TITLE: **Antisense** modulation of tumor necrosis factor receptor-1 (**TNFR1**) expression for treatment of diseases
INVENTOR(S): Baker, Brenda F.; Cowsert, Lex M.; Zhang, Hong; Dean, Nicholas M.
PATENT ASSIGNEE(S): Isis Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 121 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002048168	A1	20020620	WO 2001-US51224	20011022
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002043429	A5	20020624	AU 2002-43429	20011022

PRIORITY APPLN. INFO.: US 2000-695451 A 20001024
WO 2001-US51224 W 20011022

AB **Antisense** compds., compns. and methods are provided for modulating the expression of **TNFR1**. The compns. comprise **antisense** compds., particularly **antisense** oligonucleotides, targeted to nucleic acids encoding **TNFR1**. Methods of using these compds. for modulation of **TNFR1** expression and for treatment of diseases assocd. with expression of **TNFR1** are provided. Diseases treated were liver injury, hepatitis and liver cancer.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 5 OF 25 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2002:396966 BIOSIS
DOCUMENT NUMBER: PREV200200396966
TITLE: Identification and characterization of a novel zinc metalloproteinase that up-regulates type I tumor necrosis

factor receptor shedding.
AUTHOR(S): Cui, Xinle (1); Alsaaty, Sura; Lawrance, Marion; Combs, Christian A.; Rouhani, Farshid (1); Levine, Stewart J. (1)
CORPORATE SOURCE: (1) Pulmonary-Critical Care Medicine Branch, NHLBI, 10 Center Drive, NIH Bldg 10, Room 6D16, MSC 1590, Bethesda, MD, 20892 USA
SOURCE: FASEB Journal, (March 22, 2002) Vol. 16, No. 5, pp. A1193-A1194. http://www.fasebj.org/. print.
Meeting Info.: Annual Meeting of Professional Research Scientists on Experimental Biology New Orleans, Louisiana, USA April 20-24, 2002
ISSN: 0892-6638.
DOCUMENT TYPE: Conference
LANGUAGE: English
AB Utilizing a yeast two-hybrid approach, we have identified, cloned, and characterized a novel zinc metalloproteinase that up-regulates shedding of type I tumor necrosis factor receptor (**TNFR1**). We have named this protein Aminopeptidase Regulator of **TNFR1** Shedding (ARTS-1). ARTS-1 is a type II integral membrane protein with selective aminopeptidase activity for non-polar amino acids. ARTS-1 is expressed as a 100-kDa membrane-associated protein in human bronchial epithelial cells (HBEC) and human umbilical vein cells (HUVEC). ARTS-1 binds to **TNFR1** in vivo, as demonstrated by immunoprecipitation, but does not interact with TNFR2. A direct relationship exists between membrane-associated ARTS-1 protein levels and concordant changes in **TNFR1** shedding. Human pulmonary epithelial cell lines (NCI-H292) and HUVEC cells over-expressing ARTS-1 protein demonstrate increased **TNFR1** shedding and decreased membrane-associated **TNFR1**, while **anti-sense** ARTS-1 NCI-H292 cell lines and HUVEC cells demonstrate decreased **TNFR1** shedding and increased membrane-associated **TNFR1**. There was no change in TNFR2 shedding from the ARTS-1 cell lines, suggesting specificity of ARTS-1 towards **TNFR1**. The increased **TNFR1** shedding was inhibited by the hydroxamate-based metalloproteinase inhibitors, TAPI-0, TAPI-1, and TAPI-2. No change in TACE protein expression was noted in the ARTS-1 cell lines. We conclude that ARTS-1 is a novel metalloproteinase that binds to **TNFR1** and up-regulates its shedding.

L4 ANSWER 6 OF 25 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2002:395944 BIOSIS
DOCUMENT NUMBER: PREV200200395944
TITLE: Functional dissection of both Fas and **TNFR1** apoptotic signaling pathways in mouse liver using **antisense** oligonucleotides.
AUTHOR(S): Zhang, Hong (1); Luther, Doreen (1); Conklin, Boyd (1); Lemonidis, Kristina (1); Bennett, C. Frank (1); Freier, Sue (1); Dean, Nicholas M. (1)
CORPORATE SOURCE: (1) Isis Pharmaceuticals, Carlsbad, CA USA
SOURCE: Proceedings of the American Association for Cancer Research Annual Meeting, (March, 2002) Vol. 43, pp. 711. print.
Meeting Info.: 93rd Annual Meeting of the American Association for Cancer Research San Francisco, California, USA April 06-10, 2002
ISSN: 0197-016X.
DOCUMENT TYPE: Conference
LANGUAGE: English

L4 ANSWER 7 OF 25 MEDLINE DUPLICATE 4
ACCESSION NUMBER: 2002438438 MEDLINE
DOCUMENT NUMBER: 22176770 PubMed ID: 12189246
TITLE: Identification of ARTS-1 as a novel **TNFR1**-binding protein that promotes **TNFR1** ectodomain shedding.

AUTHOR: Cui Xinle; Hawari Feras; Alsaaty Sura; Lawrence Marion; Combs Christian A; Geng Weidong; Rouhani Farshid N; Miskinis Dianne; Levine Stewart J
CORPORATE SOURCE: Pulmonary-Critical Care Medicine Branch, National Heart, Lung, and Blood Institute, , National Institutes of Health, Bethesda, Maryland 20892-1590, USA.
SOURCE: JOURNAL OF CLINICAL INVESTIGATION, (2002 Aug) 110 (4) 515-26.
Journal code: 7802877. ISSN: 0021-9738.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
OTHER SOURCE: GENBANK-AF222340
ENTRY MONTH: 200209
ENTRY DATE: Entered STN: 20020829
Last Updated on STN: 20020907
Entered Medline: 20020906

AB Proteolytic cleavage of **TNF receptor 1** (**TNFR1**) generates soluble receptors that regulate TNF bioactivity. We hypothesized that the mechanism of **TNFR1** shedding might involve interactions with regulatory ectoproteins. Using a yeast two-hybrid approach, we identified ARTS-1 (aminopeptidase regulator of **TNFR1** shedding) as a type II integral membrane protein that binds to the **TNFR1** extracellular domain. In vivo binding of membrane-associated ARTS-1 to **TNFR1** was confirmed by coimmunoprecipitation experiments using human pulmonary epithelial and umbilical vein endothelial cells. A direct relationship exists between membrane-associated ARTS-1 protein levels and concordant changes in **TNFR1** shedding. Cells overexpressing ARTS-1 demonstrated increased **TNFR1** shedding and decreased membrane-associated **TNFR1**, while cells expressing **antisense** ARTS-1 mRNA demonstrated decreased membrane-associated ARTS-1, decreased **TNFR1** shedding, and increased membrane-associated **TNFR1**. ARTS-1 neither bound to TNFR2 nor altered its shedding, suggesting specificity for **TNFR1**. Although a recombinant ARTS-1 protein demonstrated selective aminopeptidase activity toward nonpolar amino acids, multiple lines of negative evidence suggest that ARTS-1 does not possess **TNFR1** sheddase activity. These data indicate that ARTS-1 is a multifunctional ectoprotein capable of binding to and promoting **TNFR1** shedding. We propose that formation of a **TNFR1** -ARTS-1 molecular complex represents a novel mechanism by which **TNFR1** shedding is regulated.

L4 ANSWER 8 OF 25 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2002444410 EMBASE
TITLE: Pharmacogenomics of response to anti-tumor necrosis factor therapy in patients with Crohn's disease.
AUTHOR: Shetty A.; Forbes A.
CORPORATE SOURCE: Dr. A. Forbes, St Mark's Hosp./Academic Institute, Watford Road, Harrow, HA1 3UJ, United Kingdom.
alastair.forbes@ic.ac.uk
SOURCE: American Journal of PharmacoGenomics, (2002) 2/4 (215-221).
Refs: 50
ISSN: 1175-2203 CODEN: AJPMC8
COUNTRY: New Zealand
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 022 Human Genetics
030 Pharmacology
036 Health Policy, Economics and Management
037 Drug Literature Index
048 Gastroenterology

LANGUAGE: English
SUMMARY LANGUAGE: English

AB The relatively recent development of genetically engineered agents has the potential to alter the treatment of Crohn's disease radically, and drugs that inhibit tumor necrosis factor-.alpha. (TNF.alpha.) have been introduced as a new therapeutic class with high efficacy, rapid onset of action, prolonged effect, and improved tolerance. However these agents are expensive and at least one-third of the eligible patients fail to show any useful response. Finding a means to predict those who will respond, and to anticipate relapse are, therefore, of obvious importance. T helper-type 1 (Th1) lymphocytes orchestrate much of the inflammation in Crohn's disease mainly via production of TNF.alpha., which appears to play a pivotal role as a pro-inflammatory cytokine. It exerts its effects through its own family of receptors (**TNFR1** and TNFR2), the end results of which include apoptosis, c-Jun N-terminal kinase/stress-activated protein kinase (JNK/SAPK) activation and NF-.kappa.B activation. Activated NF-.kappa.B enters the nucleus and induces transcription of genes associated with inflammation, host defense and cell survival. The promoter region of the TNF gene lies between nucleotides -1 and -1300, and encompasses numerous polymorphic sites associated with potential binding sites for various transcription factors. Carriers of the TNF allele 2 (TNF2), which contains a single base-pair polymorphism at the -308 promoter position, produce slightly more TNF.alpha. in their intestinal mucosa than non-TNF2 carriers. TNF polymorphisms also appear to influence the nature and frequency of extraintestinal manifestations of inflammatory bowel disease (IBD). A number of routes of inhibition of TNF are being investigated. Most extensively evaluated is the use of monoclonal antibodies against TNF.alpha. (e.g. infliximab). Several large controlled trials indicate that infliximab has a role in treating patients with moderate to severely active Crohn's disease and in fistulating Crohn's disease. Although it would be useful to genetically differentiate 'responders' from 'non-responders,' currently there are few published data on TNF polymorphisms in IBD, and often only selected polymorphisms are genotyped. Small studies have shown possible associations between poor response to infliximab and increasing mucosal levels of activated NF-.kappa.B, homozygosity for the polymorphism in exon 6 of TNFR2 (genotype Arg196Arg), positivity for perinuclear antineutrophil cytoplasmic antibodies (ANCA), and with the presence of increased numbers of activated lamina propia mononuclear cells producing interferon-.gamma. and TNF.alpha.. This is a rapidly changing field, and more information of greater direct clinical benefit can be expected soon.

L4 ANSWER 9 OF 25 MEDLINE DUPLICATE 5
ACCESSION NUMBER: 2002240920 MEDLINE
DOCUMENT NUMBER: 21974858 PubMed ID: 11978013
TITLE: Stable inhibition of NF-kappa B in salivary gland cells does not enhance sensitivity to TNF-alpha-induced apoptosis due to upregulation of TRAF-1 expression.
AUTHOR: Aota Keiko; Azuma Masayuki; Tamatani Tetsuya; Yamashita Tsuyoshi; Ashida Yuki; Sato Mitsunobu
CORPORATE SOURCE: Second Department of Oral and Maxillofacial Surgery, Tokushima University School of Dentistry, 3 Kuramoto-cho, Tokushima 770-8504, Japan.. azumasa@dent.tokushima-u.ac.jp
SOURCE: EXPERIMENTAL CELL RESEARCH, (2002 May 15) 276 (1) 111-9. Journal code: 0373226. ISSN: 0014-4827.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200205
ENTRY DATE: Entered STN: 20020430
Last Updated on STN: 20020602

Entered Medline: 20020531

AB The transcription factor NF-kappa B inhibits the apoptotic response induced by TNF-alpha. However, in salivary gland cell clones (ACMT-6 and ACMT-7) in which NF-kappa B activation was suppressed by introduction of a super-repressor form of I kappa B-alpha cDNA, TNF-alpha did not cause apoptosis. Thus, to investigate the molecular mechanism involved in the unresponsiveness of these cell clones to TNF-alpha-induced apoptosis, we examined the effect of TNF-alpha on the expression of antiapoptotic proteins, including TNF receptor-associated factor (TRAF)-1, TRAF-2, cellular inhibitor of apoptosis protein (cIAP)-1, and cIAP-2. Here we show that expression of TRAF-1 was commonly detected by treatment with TNF-alpha in ACMT-6, ACMT-7, and an empty vector-transfected cell clone (ACpRc-1) and that downregulation of TRAF-1 protein by either treatment with an **antisense** oligonucleotide or introduction of an **antisense** plasmid resulted in the induction of apoptosis in these cell clones. Our results, therefore, suggest that one of the mechanisms by which cells acquire resistance to TNF-alpha-induced apoptosis is a TNF-alpha induction of TRAF-1.

L4 ANSWER 10 OF 25 CA COPYRIGHT 2003 ACS
ACCESSION NUMBER: 137:308589 CA
TITLE: Tumor Necrosis Factor-Alpha Effects on Rat Gastric Enterochromaffin-Like Cells
AUTHOR(S): Huber, Christian; Zanner, Robert; Pohlinger, Agnes; Mahr, Sabine; Neu, Bruno; Prinz, Christian
CORPORATE SOURCE: Department of Medicine II, Technical University of Munich, Germany
SOURCE: Digestion (2002), 65(2), 87-102
CODEN: DIGEBW; ISSN: 0012-2823
PUBLISHER: S. Karger AG
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Gastric enterochromaffin-like (ECL) cells are histamine-producing cells in the gastric epithelium which are responsible for the peripheral regulation of acid secretion. The gastric mucosa is frequently infected with Helicobacter pylori, leading to increased levels of the pro-inflammatory cytokine tumor necrosis factor-.alpha. (TNF-.alpha.). The aim of our current study was to identify the effect of TNF-.alpha. on programmed cell death. ECL cells were isolated from the rat corpus mucosa to a purity >90%. TNF receptor and adapter protein presence were detd. using RT-PCR, Western blot and immunocytochem. Apoptosis was measured by Tdt-mediated dUTP nick end labeling reaction and by DNA fragmentation based ELISA. Isolated ECL cells were found to express the TNF receptor p55 and IFN-.gamma. receptor, but not the TNF receptor p75 or CD95. TNF-.alpha. (25 ng/mL) increased apoptosis in ECL cells approx. 4-fold, IFN-.gamma. had no effect. Western blot anal. revealed that TNF-.alpha. caused degrdn. of I.kappa.B.alpha. within 10 min. EMSA demonstrated that TNF-.alpha. led to increased DNA-binding activity of NF.kappa.B and that proteasome inhibitors counteracted NF.kappa.B activation. Proteasome inhibitors, specific **antisense** oligodeoxynucleotides against the p65 subunit of the NF.kappa.B complex and the NO synthase inhibitor NG-monomethyl-L-Arg completely prevented TNF-.alpha.-induced apoptosis. These data suggest that TNF-.alpha. induces apoptosis of isolated gastric ECL cells via activation of NF.kappa.B and the generation of NO.

REFERENCE COUNT: 67 THERE ARE 67 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 11 OF 25 CA COPYRIGHT 2003 ACS
ACCESSION NUMBER: 135:238607 CA
TITLE: Cloning, characterization and therapeutic applications of ARTS-1, sheddase of **TNF** type I **receptor** and other cytokine receptors

INVENTOR(S): Levine, Stewart
PATENT ASSIGNEE(S): Government of the United States of America, as Represented by the Secretary, Department of Health and Human Services, USA
SOURCE: PCT Int. Appl., 139 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001064856	A2	20010907	WO 2001-US6464	20010228
WO 2001064856	A3	20020418		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

AU 2001045371	A5	20010912	AU 2001-45371	20010228

PRIORITY APPLN. INFO.: US 2000-185586P P 20000228
WO 2001-US6464 W 20010228

AB The present invention provides compns. and methods for the regulation of cytokine signaling through the tumor necrosis factor (TNF) pathway. Specifically, the invention provides a novel gene, polypeptide and related compns. and methods for the regulation of ectodomain shedding. Specifically, the invention provides a novel polypeptide and a gene which encodes the polypeptide, which has the ability to promote the shedding of the extracellular domain of type I TNF receptor (**TNFR1**). This polypeptide and gene are called ARTS-1, for aminopeptidase regulator of type I, 55 kDa TNF receptor ectodomain shedding. Cloning, amino acid and encoding cDNA sequences of human ARTS-1 are disclosed. The open reading frame predicted from the human ARTS-1 cDNA encodes a protein of 941 amino acid residues. The patterns of tissue expression of the endogenous ARTS-1 and recombinant ARTS-1 expression in cultured cell lines are described. ARTS-1 **TNFR1** ectodomain sheddase regulatory activity is analyzed. It is contemplated that ARTS-1 will also regulate the shedding of ectodomains of other cytokine receptors including IL-1RII and IL-6R. In preferred embodiments, methods and compns. for the regulation of **TNFR1** ectodomain shedding are provided. The present invention finds use in therapeutics, diagnostics, and drug screening applications.

L4 ANSWER 12 OF 25 MEDLINE
ACCESSION NUMBER: 2001293704 MEDLINE
DOCUMENT NUMBER: 21264483 PubMed ID: 11278725
TITLE: Phosphorylation of the tumor necrosis factor receptor CD120a (p55) recruits Bcl-2 and protects against apoptosis.
AUTHOR: Cottin V; Van Linden A A; Riches D W
CORPORATE SOURCE: Program in Cell Biology, Department of Pediatrics, National Jewish Medical and Research Center, Denver, Colorado 80206, USA.
CONTRACT NUMBER: HL 56556 (NHLBI)
HL55549 (NHLBI)
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (2001 May 18) 276 (20) 17252-60.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200107
ENTRY DATE: Entered STN: 20010709
Last Updated on STN: 20030105
Entered Medline: 20010705

AB Ligation of the tumor necrosis factor alpha receptor CD120a initiates responses as diverse as apoptosis and the expression of NF-kappaB-dependent pro-survival genes. How these opposing responses are controlled remains poorly understood. Here we demonstrate that phosphorylation by p42(mapk/erk2) inhibits the apoptotic activity of CD120a while preserving its ability to activate NF-kappaB. Phosphorylated CD120a is re-localized from the Golgi complex to tubular structures of the endoplasmic reticulum wherein it recruits Bcl-2. **Antisense** -mediated down-regulation of Bcl-2 antagonized the localization of CD120a to tubular structures and reversed the protection from apoptosis conferred by receptor phosphorylation. We propose that phosphorylation of CD120a represents a novel, Bcl-2-dependent mechanism by which the apoptotic activity of the receptor may be regulated. Thus, oncogenic activation of p42(mapk/erk2) may serve to inhibit the apoptotic activity of this death receptor while preserving NF-kappaB-dependent responses and may thus indirectly contribute to a failure to eliminate cells bearing oncogenes of the Ras-Raf-MEK-p42(mapk/erk2) pathway.

L4 ANSWER 13 OF 25 SCISEARCH COPYRIGHT 2003 THOMSON ISI
ACCESSION NUMBER: 2001:144561 SCISEARCH
THE GENUINE ARTICLE: 398YW
TITLE: Hyaluronidase induction of a WW domain-containing oxidoreductase that enhances tumor necrosis factor cytotoxicity
AUTHOR: Chang N S (Reprint); Pratt N; Heath J; Schultz L; Sleve D; Carey G B; Zevotek N
CORPORATE SOURCE: Guthrie Res Inst, Lab Mol Immunol, 1 Guthrie Sq, Sayre, PA 18840 USA (Reprint); Guthrie Res Inst, Lab Mol Immunol, Sayre, PA 18840 USA
COUNTRY OF AUTHOR: USA
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (2 FEB 2001) Vol. 276, No. 5, pp. 3361-3370.
Publisher: AMER SOC BIOCHEMISTRY MOLECULAR BIOLOGY INC, 9650 ROCKVILLE PIKE, BETHESDA, MD 20814 USA.
ISSN: 0021-9258.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 49

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB To determine how hyaluronidase increases certain cancer cell sensitivity to tumor necrosis factor (TNF) cytotoxicity, we report here the isolation and characterization of a hyaluronidase-induced murine WW domain-containing oxidoreductase (WOX1), WOX1 is composed of two N-terminal WW domains, a nuclear localization sequence, and a C-terminal alcohol dehydrogenase (ADH) domain. WOX1 is mainly located in the mitochondria, and the mitochondrial targeting sequence was mapped within the ADH domain. Induction of mitochondrial permeability transition by TNF, staurosporine, and atractyloside resulted in WOX1 release from mitochondria and subsequent nuclear translocation, TNF-mediated WOX1 nuclear translocation occurred shortly after that of nuclear factor-kappaB nuclear translocation, whereas both were independent events. WOX1 enhanced TNF cytotoxicity in L929 cells via its WW and ADH domains as determined using stable cell transfectants, In parallel with this observation, WOX1 also enhanced TRADD (TNF receptor-associated death domain protein)-mediated cell death in transient expression experiments.

Antisense expression of WOX1 raised TNF resistance in L929 cells. Enhancement of TNF cytotoxicity by WOX1 is due, in part, to its significant downregulation of the apoptosis inhibitors Bcl-2 and Bcl-x(L) (>85%), but up-regulation of pro-apoptotic p53 (similar to 200%) by the ADH domain. When overexpressed, the ADH domain mediated apoptosis, probably due to modulation of expression of these proteins. The WW domains failed to modulate the expression of these proteins, but sensitized COS-7 cells to TNF killing and mediated apoptosis in various cancer cells independently of caspases, Transient cotransfection of cells with both p53 and WOX1 induced apoptosis in a synergistic manner. WOX1 colocalizes with p53 in the cytosol and binds to the proline-rich region of p53 via its WW domains. Blocking of WOX1 expression by **antisense** mRNA abolished p53 apoptosis, Thus, WOX1 is a mitochondrial apoptogenic protein and an essential partner of p53 in cell death.

L4 ANSWER 14 OF 25 MEDLINE
ACCESSION NUMBER: 2001262281 MEDLINE
DOCUMENT NUMBER: 21221416 PubMed ID: 11324713
TITLE: Induction of tumor necrosis factor receptor type 2 gene expression by tumor necrosis factor-alpha in rat primary astrocytes.
AUTHOR: Lung H L; Leung K N; Stadlin A; Ma C M; Tsang D
CORPORATE SOURCE: Department of Biochemistry, The Chinese University of Hong Kong, Shatin, NT.
SOURCE: LIFE SCIENCES, (2001 Mar 23) 68 (18) 2081-91.
Journal code: 0375521. ISSN: 0024-3205.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200105
ENTRY DATE: Entered STN: 20010521
Last Updated on STN: 20010521
Entered Medline: 20010517

AB Using reverse transcription-polymerase chain reaction (RT-PCR) technique, the messenger RNA (mRNA) for tumor necrosis factor receptor type 2 (TNF-R2, 75/80 kDa) was detected in rat primary astrocytes, with much lower level of expression when compared to that for tumor necrosis factor **receptor** type **1** (**TNF**-R1, 55/60 kDa). Upon exposure to TNF-alpha (100 U/ml), the TNF-R2 mRNA level was greatly enhanced at 8 h, while TNF-R1 mRNA remained unchanged even after 24 h. The induction of TNF-R2 gene expression by TNF-alpha was dose-dependent and seemed to be unique to TNF-alpha, as interleukin-6 (IL-6) had no significant effect on TNF-R2 expression. Since TNF-R2 was reported to mediate mitogenic and gene-inducing effects in many other cell types, it is likely that the reported proliferative effect of TNF-alpha on astrocytes was also mediated by this TNF receptor subtype. Upon exposure to TNF-alpha or lipopolysaccharide (LPS), the expression of TNF-alpha gene was induced, and the LPS-induced TNF-alpha seemed to selectively enhance the TNF-R2 gene expression. Collectively, our results suggest that the TNF-alpha or LPS-induced expression of both TNF-R2 and TNF-alpha may provide a positive control mechanism to further enhance the proliferative effect of TNF-alpha in astrocytes.

L4 ANSWER 15 OF 25 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2001:256810 BIOSIS
DOCUMENT NUMBER: PREV200100256810
TITLE: p62/ZIP plays a role in regulation of NGF-mediated NF-kappaB activation.
AUTHOR(S): Paulk, Jessica M. (1); Wooten, Marie W. (1)
CORPORATE SOURCE: (1) Auburn University, 331 Funchess Hall, Auburn, AL, 36849 USA

SOURCE: FASEB Journal, (March 8, 2001) Vol. 15, No. 5, pp. A1163. print.
Meeting Info.: Annual Meeting of the Federation of American Societies for Experimental Biology on Experimental Biology 2001 Orlando, Florida, USA March 31-April 04, 2001
ISSN: 0892-6638.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Zeta Protein kinase C interacting protein, p62/ZIP, is part of the transcription factor nuclear factor-kappa B (NF-kappaB) for both IL-**1** and **TNF receptors**. NF-kappa B is activated by nerve growth factor (NGF) treatment of pheochromocytoma (PC12) cells. We hypothesized that p62 may serve to regulate NGFs properties. To test this hypothesis, p62 was overexpressed or **antisense** p62 was used to deplete cells of p62 protein via transient transfection. After stimulating the transfected cells with NGF, survivability, differentiation and NF-kappa B activation were examined. Cells overexpressing p62 displayed enhanced survival compared to control cells in a serum free environment. By comparison transfection of **antisense** p62 decreased survival compared to control. Effects of p62 on NGF-induced neurite outgrowth were determined. p62 overexpression enhanced neurite outgrowth compared to control cells, whereas those cells transfected with **antisense** p62 displayed reduction in neurites. In addition, p65 ReIA translocation to the nucleus was examined by both immunostaining and a kappa B reporter assay. Transfection of increasing concentrations of p62 into PC12 cells enhanced NGF-induced NF-kappa B activity in a dose-dependent manner. By comparison, p62 blocked NGF induced NF-kappa B activity. Together, these results reveal that p62 plays a crucial role in both NF-kappa B activation coupled to survival and differentiation of PC12 cells.

L4 ANSWER 16 OF 25 MEDLINE DUPLICATE 6
ACCESSION NUMBER: 2001170624 MEDLINE
DOCUMENT NUMBER: 21100485 PubMed ID: 11165872
TITLE: Genes regulated in human breast cancer cells overexpressing manganese-containing superoxide dismutase.
AUTHOR: Li Z; Khaletskiy A; Wang J; Wong J Y; Oberley L W; Li J J
CORPORATE SOURCE: Department of Radiation Research, Beckman Research Institute, City of Hope National Medical Center, 1500 Duarte Road, Duarte, CA 91010-3000, USA.
SOURCE: FREE RADICAL BIOLOGY AND MEDICINE, (2001 Feb 1) 30 (3) 260-7.
Journal code: 8709159. ISSN: 0891-5849.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200104
ENTRY DATE: Entered STN: 20010502
Last Updated on STN: 20010502
Entered Medline: 20010426

AB The mitochondrial antioxidant enzyme manganese-containing superoxide dismutase (MnSOD) functions as a tumor suppressor gene. Reconstitution of MnSOD expression in several human cancer cell lines leads to reversion of malignancy and induces a resistant phenotype to the cytotoxic effects of TNF and hyperthermia. The signaling pathways that underlie these phenotypic changes in MnSOD-overexpressing cells are unknown, although alterations in the activity of several redox-sensitive transcription factors, including AP-1 and NF-kappaB, have been observed. To determine the downstream signaling molecules involved in MnSOD-induced cell resistant phenotype, in the present study we analyzed the expression

profile of several groups of genes related to stress response, DNA repair, and apoptosis, in a human breast cancer MCF-7 cell line overexpressing MnSOD (MCF+SOD). Of 588 genes examined, 5 (0.85%) were up-regulated (2-42-fold), and 11 (1.9%) were down-regulated (2-33-fold) in the MCF+SOD cells compared to the parental MCF-7 cells. The five up-regulated genes were MET, GADD153, CD9, alpha-catenin and plakoglobin. The genes with the most significant down-regulation included: vascular endothelial growth factor **receptor 1**, **TNF**-alpha converting enzyme, and interleukin-1beta. GADD153 (involved in the repair of DNA double strand breaks) showed a 33-fold increase in microarray analysis and these results were confirmed by RT-PCR. To further determine the specificity in MnSOD-induced gene regulation, MCF+SOD cells were stably transfected with an **antisense** MnSOD sequence whose expression was controlled by a tetracycline-inducible regulator. Expression of three up-regulated genes was measured after induction of **antisense** MnSOD expression. Interestingly, expression level of GADD153 but not MET or CD9 was reduced 24 h after **antisense** MnSOD induction. Together, these results suggest that reconstitution of MnSOD in tumor cells can specifically modulate the expression of down-stream effector genes. GADD153 and other elements observed in the MCF+SOD cells may play a key role in signaling the MnSOD-induced cell phenotypic change.

L4 ANSWER 17 OF 25 MEDLINE DUPLICATE 7
ACCESSION NUMBER: 2001024317 MEDLINE
DOCUMENT NUMBER: 20467514 PubMed ID: 11012883
TITLE: Mechanism of chronic obstructive uropathy: increased expression of apoptosis-promoting molecules.
AUTHOR: Choi Y J; Baranowska-Daca E; Nguyen V; Koji T; Ballantyne C M; Sheikh-Hamad D; Suki W N; Truong L D
CORPORATE SOURCE: Renal Pathology Laboratory, Department of Pathology, Department of Medicine, The Methodist Hospital and BaylorCollege of Medicine, Houston, Texas, USA.
SOURCE: KIDNEY INTERNATIONAL, (2000 Oct) 58 (4) 1481-91. Journal code: 0323470. ISSN: 0085-2538.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200011
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20001113

AB BACKGROUND: We have demonstrated that renal tubular and interstitial cells undergo pronounced apoptosis during the course of chronic obstructive uropathy (COU). Apoptosis is a complex cellular process consisting of multiple steps, each of which is mediated by families of related molecules. These families may include receptor/ligand molecules such as Fas, Fas ligand, tumor necrosis factor receptor-**1** (**TNFR-1**), and TNF-related apoptosis inducing ligand (TRAIL); signal transduction adapter molecules such as Fas-associated death domain (FADD), **TNFR-1** associated death domain (TRADD), receptor-interacting protein (RIP), Fas-associated factor (FAF), and Fas-associated phosphatase (FAP); or effector molecules such as caspases. However, the mechanism of tubular cell apoptosis, as well as the pathogenetic relevance of these apoptosis-related molecules in COU, remains poorly understood. METHODS: Kidneys were harvested from sham-operated control mice and mice with COU created by left ureter ligation sacrificed in groups of three at days 4, 15, 30, and 45. To detect apoptotic tubular and interstitial cells, in situ end labeling of fragmented DNA was performed. To detect the expression of apoptosis-related molecules, ribonuclease protection assay was used with specific **antisense** RNA probes for Fas, Fas ligand, **TNFR**

-1, TRAIL, FADD, TRADD, RIP, FAF, FAP, and caspase-8. Immunostaining for Fas, Fas ligand, TRAIL, TRADD, RIP, and caspase-8 was also performed. To assess the role of these molecules in COU-associated renal cell apoptosis, the frequencies of apoptotic tubular and interstitial cells were separately quantitated for each experimental time point, and their patterns of variation were correlated with those of apoptosis-related molecules. RESULTS: The obstructed kidneys displayed increased apoptosis of both tubular and interstitial cells. Tubular cell apoptosis appeared at day 4 after ureter ligation, peaked (fivefold of control) at day 15, and decreased gradually until the end of the experiment. In contrast, interstitial cell apoptosis sustained a progressive increase throughout the experiment. Apoptosis was minimal at all experimental time points for control and contralateral kidneys. Compared with control and contralateral kidneys, the ligated kidneys displayed a dynamic expression of mRNAs for many apoptosis-related molecules, which included an up to threefold increase for Fas, Fas ligand, TNF-R1, TRAIL, TRADD, RIP, and caspase-8, and an up to twofold increase for FADD and FAP, but there was little change for FAF. These mRNAs increased between days 4 and 15, decreased until day 30, but then increased again until day 45. The rise and fall of mRNAs between days 4 and 30 paralleled a similar fluctuation in tubular cell apoptosis in that period. The subsequent increase of mRNAs was correlated with a continuous rise of interstitial cell apoptosis. We demonstrated a positive immunostaining for Fas and Fas ligand in the tubular cells at early time points as well as in interstitial inflammatory cells at later time points. Although increased expression of TRAIL, TRADD, RIP, and caspase-8 was noted in tubular cells, there was no staining for these molecules in interstitial cells. CONCLUSION: The current study documents a dynamic expression of several molecules that are known to mediate the most crucial steps of apoptosis. It implicates these molecules in COU-associated renal cell apoptosis and in the pathogenesis of this condition. It also lays the foundation for interventional studies, including genetic engineering, to evaluate the molecular control of apoptosis associated with COU.

L4 ANSWER 18 OF 25 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE 8

ACCESSION NUMBER: 2000:277936 BIOSIS
DOCUMENT NUMBER: PREV200000277936
TITLE: **Antisense** inhibition of **TNFR1** expression.
AUTHOR(S): Baker, Brenda F. (1); Cowsert, Lex M.
CORPORATE SOURCE: (1) Carlsbad, CA USA
ASSIGNEE: Isis Pharmaceuticals Inc.
PATENT INFORMATION: US 6007995 December 28, 1999
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (Dec. 28, 1999) Vol. 1229, No. 4, pp. No pagination. e-file.
ISSN: 0098-1133.
DOCUMENT TYPE: Patent
LANGUAGE: English

AB **Antisense** compounds, compositions and methods are provided for modulating the expression of **TNFR1**. The compositions comprise **antisense** compounds, particularly **antisense** oligonucleotides, targeted to nucleic acids encoding **TNFR1**. Methods of using these compounds for modulation of **TNFR1** expression and for treatment of diseases associated with expression of **TNFR1** are provided.

L4 ANSWER 19 OF 25 CA COPYRIGHT 2003 ACS

ACCESSION NUMBER: 132:2794 CA
TITLE: Modulators affecting tumor necrosis factor receptor-releasing enzyme activity

INVENTOR(S): Gatanaga, Tetsuya; Granger, Gale A.
PATENT ASSIGNEE(S): The Regents of the University of California, USA
SOURCE: PCT Int. Appl., 106 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9958559	A2	19991118	WO 1999-US10793	19990514
WO 9958559	A3	20000120		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2328133	AA	19991118	CA 1999-2328133	19990514
AU 9939960	A1	19991129	AU 1999-39960	19990514
BR 9910458	A	20010102	BR 1999-10458	19990514
EP 1076710	A2	20010221	EP 1999-923115	19990514
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2002514402	T2	20020521	JP 2000-548361	19990514
US 2002091243	A1	20020711	US 2000-752639	20001229

PRIORITY APPLN. INFO.: US 1998-81385 A 19980514
WO 1999-US10793 W 19990514
US 2000-712813 A1 20001113

AB The biol. effects of the cytokine tumor necrosis factor (TNF) are mediated by binding to receptors on the surface of cells. Nine new proteins and polynucleotides are provided that promote enzymic cleavage and release of TNF receptors. The isolated polynucleotides have the following properties: (a) the sequence is expressed at the mRNA level in Jurkat T cells; (b) when COS-1 cells expressing **TNF-receptor** are genetically transformed to express the sequence, the cells have increased enzymic activity for cleaving and releasing the receptor. Also provided are screening methods for identifying addnl. compds. that influence TNF receptor shedding. TRRE activity alleviates septic shock and decreases tumor necrotizing activity, and the modulator expression products are effective in treating septic shock. As active ingredients in a pharmaceutical compn., the products of this invention increase or decrease TNF signal transduction, thereby alleviating the pathol. of disease.

L4 ANSWER 20 OF 25 CA COPYRIGHT 2003 ACS
ACCESSION NUMBER: 131:346559 CA
TITLE: **Antisense** modulation of sentrin expression
INVENTOR(S): Baker, Brenda F.; Cowsert, Lex M.
PATENT ASSIGNEE(S): Isis Pharmaceuticals, Inc., USA
SOURCE: U.S., 29 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

US 5985664	A	19991116	US 1998-213768	19981217
WO 2000036148	A1	20000622	WO 1999-US13205	19990610

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

AU 9946795	A1	20000703	AU 1999-46795	19990610

PRIORITY APPLN. INFO.: US 1998-213768 A 19981217
WO 1999-US13205 W 19990610

AB **Antisense** compds., compns. and methods are provided for modulating the expression of Sentrin. Sentrin (also known as UBL1, PIC1, SMP1, or SUMO-1) is a ubiquitin-like mol. which attaches to a protein but, unlike ubiquitin, conjugation results in protein trafficking and localization and not in labeling of target proteins for degrdn.; sentrin appears to binding to the death domain of the **TNFR1** receptor and play a role in apoptosis, as well as be involved in nuclear protein import. The compns. comprise **antisense** compds., particularly **antisense** oligonucleotides, targeted to nucleic acids encoding Sentrin. Phosphorothioated **antisense** oligonucleotides, as well as gapmers contg. 2'-methoxyethyl ribose modifications, yielded .gtoreq.25% inhibition of Sentrin expression. Methods of using these compds. for modulation of Sentrin expression and for treatment of diseases assocd. with expression of Sentrin are provided.

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 21 OF 25 MEDLINE

ACCESSION NUMBER: 1999286228 MEDLINE
DOCUMENT NUMBER: 99286228 PubMed ID: 10356400
TITLE: The interaction of p62 with RIP links the atypical PKCs to NF-kappaB activation.
AUTHOR: Sanz L; Sanchez P; Lallena M J; Diaz-Meco M T; Moscat J
CORPORATE SOURCE: Laboratorio Glaxo Wellcome-CSIC de Biologia Molecular y Celular, Centro de Biologia Molecular 'Severo Ochoa' (Consejo Superior de Investigaciones Cientificas-Universidad Autonoma de Madrid), Spain.
SOURCE: EMBO JOURNAL, (1999 Jun 1) 18 (11) 3044-53.
Journal code: 8208664. ISSN: 0261-4189.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199908
ENTRY DATE: Entered STN: 19990816
Last Updated on STN: 20020420
Entered Medline: 19990805

AB The two members of the atypical protein kinase C (aPKC) subfamily of isozymes (zetaPKC and lambda/iotaPKC) are involved in the control of nuclear factor kappaB (NF-kappaB) through IKKbeta activation. Here we show that the previously described aPKC-binding protein, p62, selectively interacts with RIP but not with TRAF2 in vitro and in vivo. p62 bridges the aPKCs to RIP, whereas the aPKCs link IKKbeta to p62. In this way, a signaling cascade of interactions is established from the TNF-R1 involving TRADD/RIP/p62/aPKCs/IKKbeta. These observations define a novel pathway for the activation of NF-kappaB involving the aPKCs and p62. Consistent with this model, the expression of a dominant-negative mutant

lambda/iotaPKC impairs RIP-stimulated NF-kappaB activation. In addition, the expression of either an N-terminal aPKC-binding domain of p62, or its C-terminal RIP-binding region are sufficient to block NF-kappaB activation. Furthermore, transfection of an **antisense** construct of p62 severely abrogates NF-kappaB activation. Together, these results demonstrate that the interaction of p62 with RIP serves to link the atypical PKCs to the activation of NF-kappaB by the TNFalpha signaling pathway.

L4 ANSWER 22 OF 25 MEDLINE DUPLICATE 9
ACCESSION NUMBER: 1998237061 MEDLINE
DOCUMENT NUMBER: 98237061 PubMed ID: 9577951
TITLE: Tumor necrosis factor-alpha confers resistance to hypoxic injury in the adult mammalian cardiac myocyte.
AUTHOR: Nakano M; Knowlton A A; Dibbs Z; Mann D L
CORPORATE SOURCE: Department of Medicine, Veterans Administration Medical Center, Baylor College of Medicine, Houston, Tex 77030, USA.
CONTRACT NUMBER: P50-HL-06H (NHLBI)
R29-HL-52910 (NHLBI)
SOURCE: CIRCULATION, (1998 Apr 14) 97 (14) 1392-400.
Journal code: 0147763. ISSN: 0009-7322.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199805
ENTRY DATE: Entered STN: 19980609
Last Updated on STN: 19980609
Entered Medline: 19980527

AB BACKGROUND: Previous studies in isolated cardiac myocytes have shown that tumor necrosis factor (TNF)-alpha provokes increased expression of 27- and 70-kD stress proteins as well as manganese superoxide dismutase, suggesting that TNF-alpha might play a role in mediating stress responses in the heart. METHODS AND RESULTS: To determine whether TNF-alpha stimulation would protect isolated cardiac myocytes against environmental stress, myocyte cultures were pretreated with TNF-alpha for 12 hours and then subjected to continuous hypoxic injury (O2 content, 3 to 5 ppm) for 12 hours, followed by reoxygenation. Cell injury was assessed in terms of lactic dehydrogenase (LDH) release, 45Ca2+ uptake, and MTT metabolism. Pretreatment with TNF-alpha concentrations > or = 50 U/mL significantly attenuated LDH release by hypoxic cells compared with diluent-treated hypoxic cells. Similar findings were observed with respect to 45Ca2+ uptake and MTT metabolism in TNF-alpha-pretreated cells that were subjected to prolonged hypoxia. To determine the mechanism for the TNF-alpha-induced protective effect, the cells were pretreated with heat shock protein (HSP) 72 **antisense** oligonucleotides. These studies showed that the protective effect of TNF-alpha was not inhibited by **antisense** oligonucleotides, despite use of a concentration of **antisense** that was sufficient to attenuate the TNF-alpha-induced increase in HSP 72 expression. Subsequent studies using mutated TNF ligands showed that activation of both types **1** and 2 **TNF receptors** was sufficient to confer a protective response in isolated cardiac myocytes through an as yet unknown pathway(s). CONCLUSIONS: Taken together, the above observations demonstrate that TNF-alpha pretreatment confers resistance to hypoxic stress in the adult cardiac myocyte through a novel mechanism that appears to be different from but not necessarily exclusive of the protective response conferred by HSP 72 expression.

L4 ANSWER 23 OF 25 MEDLINE DUPLICATE 10
ACCESSION NUMBER: 1998435605 MEDLINE

DOCUMENT NUMBER: 98435605 PubMed ID: 9764576
TITLE: Autocrine self-elimination of cultured ovarian cancer cells by tumour necrosis factor alpha (TNF-alpha).
AUTHOR: Simonitsch I; Krupitza G
CORPORATE SOURCE: Institute of Clinical Pathology, University of Vienna, Austria.
SOURCE: BRITISH JOURNAL OF CANCER, (1998 Oct) 78 (7) 862-70. Journal code: 0370635. ISSN: 0007-0920.
PUB. COUNTRY: SCOTLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199810
ENTRY DATE: Entered STN: 19981021
Last Updated on STN: 20000303
Entered Medline: 19981013

AB Human ovarian adenocarcinoma cells N.1 secrete an autocrine activity that stimulates active cell death under serum-reduced conditions. To substitute the autocrine activity by a single physiological component, 28 cytokines, growth factors and biomodulators were tested [interleukin 1alpha (IL-1alpha), IL-1beta, IL-2, IL-3, IL-4, IL-6, IL-10, IL-11, stem cell factor (SCF), platelet-derived growth factor (PDGF), acid fibroblast growth factor (aFGF), basic fibroblast growth factor (bFGF), insulin-like growth factor (IGF-1), IGF-2, insulin, macrophage colony-stimulating factor (M-CSF), granulocyte colony-stimulating factor (G-CSF), granulocyte-macrophage colony-stimulating factor (GM-CSF), oncostatin, RANTES (regulated on activation normal T cell expressed and secreted), angiogenin, leukaemia inhibitory factor (LIF), erythropoietin (EPO), interferon alpha (INF-alpha), INF-gamma, transferrin, tumour necrosis factor alpha (TNF-alpha, TNF-beta and bovine serum albumin for control reasons]. In these experiments, only TNF-alpha and TNF-beta rapidly induced apoptosis. TNF-alpha and **TNF-receptor 1** were expressed by N.1 cells, and the secretion of TNF-alpha was verified by enzyme-linked immunosorbent assay (ELISA). Autocrine factor-triggered apoptosis was inhibited when conditioned supernatant was preincubated with anti-TNF-alpha antibody. These findings suggested that the apoptosis-inducing component of the N.1 autocrine activity was TNF-alpha. In the presence of **antisense** c-myc oligonucleotides, induction of cell death by autocrine factor was partly inhibited. Autocrine factor and TNF-alpha stimulated transcription of the invasiveness-related protease plasminogen activator/urokinase mRNA (upa) with similar kinetics. When N.1 cells were exposed to purified plasminogen activator/urokinase protein (uPA), cell matrix contact was disrupted. Thus, uPA might serve a physiological role during TNF-induced apoptosis by affecting the interactions between cells and the basal membrane, thereby facilitating anoikis. This mechanistic study, which was restricted to a single human ovarian carcinoma model cell line (N.1), provides evidence that N.1 maintains the capacity to undergo c-myc-dependent apoptosis by the TNF-TNF-receptor pathway, and no additional pharmacological stimuli for induction of apoptosis are required.

L4 ANSWER 24 OF 25 MEDLINE DUPLICATE 11
ACCESSION NUMBER: 97166205 MEDLINE
DOCUMENT NUMBER: 97166205 PubMed ID: 9013604
TITLE: Inhibition of p75 tumor necrosis factor receptor by **antisense** oligonucleotides increases hypoxic injury and beta-amyloid toxicity in human neuronal cell line.
AUTHOR: Shen Y; Li R; Shiosaki K
CORPORATE SOURCE: Neuroscience Department, Pharmaceutical Discovery Division, Abbott Laboratories, Abbott Park, Illinois 60064-3500, USA.. Shen.Yong@igate.abbott.com

SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1997 Feb 7) 272 (6) 3550-3.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199704
ENTRY DATE: Entered STN: 19970414
Last Updated on STN: 19970414
Entered Medline: 19970402

AB Recent evidence indicates that tumor necrosis factor-alpha (TNF-alpha) is up-regulated following brain injury and in neurodegenerative disorders such as stroke, multiple sclerosis, Parkinson's disease, and Alzheimer's disease. TNF-alpha elicits its biological effects through two distinct TNF receptor (TNFR) subtypes: p55 TNFR (**TNFR1**) and p75 TNFR (TNFR2). Studies have demonstrated that the p55 TNFR contributes to cell death, whereas the role of the p75 TNFR in neuronal viability is unclear. To better understand the role of p75 TNFR, we treated human neuronal SH-SY5Y cells with phosphorothioate-modified **antisense** oligonucleotides (ASO) for p75 TNFR and established that ASO inhibited p75 TNFR expression. Treatment of SH-SY5Y cells with ASO alone did not affect cell viability, whereas treatment with both ASO and human TNF-alpha significantly increased cell death relative to treatment with TNF-alpha alone. Moreover, addition of ASO significantly increased the level of cell injury observed following hypoxic conditions or exposure of beta-amyloid peptide. These results indicate that inhibition of p75 TNFR using ASO increases the vulnerability of neurotypic cells to insults and suggest that the p75 TNFR may not be required for normal neuronal cell viability but rather plays a protective role following injury.

L4 ANSWER 25 OF 25 MEDLINE DUPLICATE 12
ACCESSION NUMBER: 94014372 MEDLINE
DOCUMENT NUMBER: 94014372 PubMed ID: 8409402
TITLE: Overexpression of major heat shock protein hsp70 inhibits tumor necrosis factor-induced activation of phospholipase A2.
AUTHOR: Jaattela M
CORPORATE SOURCE: Department of Tumor Cell Biology, Danish Cancer Society Research Center, Copenhagen.
SOURCE: JOURNAL OF IMMUNOLOGY, (1993 Oct 15) 151 (8) 4286-94.
Journal code: 2985117R. ISSN: 0022-1767.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199311
ENTRY DATE: Entered STN: 19940117
Last Updated on STN: 19940117
Entered Medline: 19931109

AB We have recently shown that major heat shock protein (hsp70) protects WEHI-S tumor cells from the cytotoxicity mediated by TNF. In the present study, the mechanism of hsp70-associated TNF resistance was investigated. Overexpression of human hsp70 or inhibition of endogenous hsp70 synthesis by expression of **antisense** hsp70 RNA did not change the ability of WEHI-S tumor cells to bind TNF or internalize and degrade the receptor-bound TNF. Moreover, TNF-induced activation of NF-kappa B-like transcription factors was unaffected by altered levels of hsp70 as tested by electrophoretic mobility shift assay. Thus, it is unlikely that the resistance is due to changes in TNF receptors or in their ability to transduce signals leading to the regulation of genes, whose expression is regulated by NF-kappa B-like transcription factors. The idea that

hsp70-associated TNF resistance is independent of regulation of TNF-induced gene expression was further supported by the results showing that hsp70 protected WEHI-S cells from TNF-mediated killing also in the presence of inhibitors of either translation or transcription. Interestingly, TNF-induced activation of arachidonic acid metabolism correlated directly with their sensitivity to TNF and inversely with the amount of hsp70 in the cells. Furthermore, TNF-induced activation of arachidonic acid metabolism was inhibited in WEHI-S cells and two TNF-sensitive human cell lines by induction of the synthesis of endogenous heat shock proteins by heat shock. Even stronger inhibition of arachidonic acid metabolism was seen in WEHI cells rendered TNF-resistant by culturing them in the presence of increasing concentrations of TNF. These cells also had reduced numbers of type **1 TNF receptors**. Overexpression of a low molecular weight heat shock protein hsp27 in WEHI-S cells had no effect on any of the parameters studied. These results show that both hsp70-mediated and TNF-induced TNF resistance are associated with a reduced activation of phospholipase A2 suggesting that phospholipase A2 plays an essential role in TNF-mediated cytotoxicity and that hsp70 interferes with the signal transduction pathway leading to its activation.

NCBI results of BLAST

BLASTN 2.2.6 [Apr-09-2003]

Reference:
Altschul, Stephen F., Thomas L. Madden, Alejandro A. Schäffer, Jinghui Zhang, Zheng Zhang, Webb Miller, and David J. Lipman (1997), "Gapped BLAST and PSI-BLAST: a new generation of protein database search programs", Nucleic Acids Res. 25:3389-3402.

RID: 1057798349-03793-16247

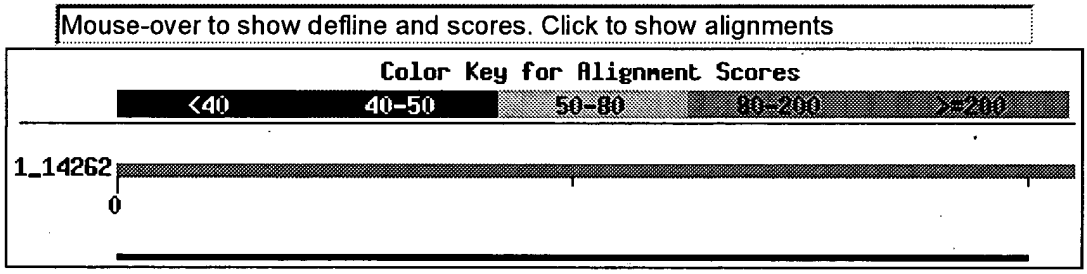
Query=
(21 letters)

Database: All GenBank+EMBL+DDBJ+PDB sequences (but no EST, STS, GSS, or phase 0, 1 or 2 HTGS sequences)
1,835,111 sequences; 8,588,587,986 total letters

If you have any problems or questions with the results of this search please refer to the **BLAST FAQs**

Taxonomy reports

Distribution of 9 Blast Hits on the Query Sequence



Sequences producing significant alignments:		Score (bits)	E Value
gi|37223|emb|X55313.1|HSTNFR1A	H.sapiens TNF-R mRNA for tum...	42	7e-09

Alignments

Get selected sequences | Select all | Deselect all

☐ >gi|37223|emb|X55313.1|HSTNFR1A H.sapiens TNF-R mRNA for tumor necrosis factor receptor type
Length = 2161

Score = 42.1 bits (21), Expect = 7e-09
Identities = 21/21 (100%)
Strand = Plus / Minus

```
Query: 1   cacggtggagaggcccatgcc 21
           ||||||||||||||||||||
Sbjct: 273 cacggtggagaggcccatgcc 253
```

Score = 16.4 bits (8), Expect = 0.39
Identities = 8/8 (100%)
Strand = Plus / Plus

```
Query: 4   ggtggaga 11
           ||||||||
Sbjct: 1341 ggtggaga 1348
```

Score = 16.4 bits (8), Expect = 0.39
Identities = 8/8 (100%)
Strand = Plus / Plus

```
Query: 2   acggtgga 9
           ||||||||
Sbjct: 966 acggtgga 973
```

Score = 16.4 bits (8), Expect = 0.39
Identities = 8/8 (100%)
Strand = Plus / Plus

```
Query: 4   ggtggaga 11
           ||||||||
Sbjct: 588 ggtggaga 595
```

Score = 16.4 bits (8), Expect = 0.39
Identities = 8/8 (100%)
Strand = Plus / Plus

```
Query: 8   gagaggcc 15
           ||||||||
Sbjct: 235 gagaggcc 242
```

Score = 14.4 bits (7), Expect = 1.5
Identities = 7/7 (100%)
Strand = Plus / Minus

```
Query: 4    ggtggag 10
           |||||||
Sbjct: 1149 ggtggag 1143
```

```
 Score = 14.4 bits (7), Expect = 1.5
 Identities = 7/7 (100%)
 Strand = Plus / Minus


Query: 1   cacggtg 7
           |||||||
Sbjct: 750 cacggtg 744



 Score = 14.4 bits (7), Expect = 1.5
 Identities = 7/7 (100%)
 Strand = Plus / Minus


Query: 7   ggagagg 13
           |||||||
Sbjct: 726 ggagagg 720



 Score = 14.4 bits (7), Expect = 1.5
 Identities = 7/7 (100%)
 Strand = Plus / Minus


Query: 1   cacggtg 7
           |||||||
Sbjct: 627 cacggtg 621
```

Get selected sequences | Select all | Deselect all

```
  Database: All GenBank+EMBL+DDBJ+PDB sequences (but no EST, STS, GSS,
  or phase 0, 1 or 2 HTGS sequences)
    Posted date:  Jul 9, 2003  1:03 AM
  Number of letters in database: -24,401,480
  Number of sequences in database:  1,826,982

Lambda     K      H
   1.37    0.711     1.31

Gapped
Lambda     K      H
   1.37    0.711     1.31


Matrix: blastn matrix:1 -3
Gap Penalties: Existence: 5, Extension: 2
Number of Hits to DB: 9
Number of Sequences: 8129
Number of extensions: 9
Number of successful extensions: 9
Number of sequences better than 1000.0: 1
Number of HSP's better than 1000.0 without gapping: 1
Number of HSP's successfully gapped in prelim test: 0
Number of HSP's that attempted gapping in prelim test: 0
Number of HSP's gapped (non-prelim): 9
```

```
length of query: 21
length of database: 2161
effective HSP length: 6
effective length of query: 15
effective length of database: 2155
effective search space:    32325
effective search space used:    32325
T: 0
A: 0
X1: 3 ( 5.9 bits)
X2: 15 (29.7 bits)
S1: 12 (24.3 bits)
S2: 3 ( 6.4 bits)
```